IGF1 neuronal response in the absence of MECP2 is dependent on TRalpha 3.

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Public Summary:
Insulin growth factor 1 (IGF1) is already in clinical trials for Rett syndrome and autism. In this publication, we showed that IGF1 interacts with the receptor of the thyroid hormone to increase neurite outgrowth. Thus, we have revealed a novel potential mechanism to explain how IGF1 works to rescue neuronal defects in Rett syndrome.

Scientific Abstract:
Rett syndrome (RTT) is an X-linked neurodevelopmental disorder in which the MECP2 (methyl CpG-binding protein 2) gene is mutated. Recent studies showed that RTT-derived neurons have many cellular deficits when compared to control, such as: less synapses, lower dendritic arborization and reduced spine density. Interestingly, treatment of RTT-derived neurons with Insulin-like Growth Factor 1 (IGF1) could rescue some of these cellular phenotypes. Given the critical role of IGF1 during neurodevelopment, the present study used human induced pluripotent stem cells (iPSCs) from RTT and control individuals to investigate the gene expression profile of IGF1 and IGF1R on different developmental stages of differentiation. We found that the thyroid hormone receptor (TRalpha 3) has a differential expression profile. Thyroid hormone is critical for normal brain development. Our results showed that there is a possible link between IGF1/IGF1R and the TRalpha 3 and that over expression of IGF1R in RTT cells may be the cause of neurites improvement in neural RTT-derived neurons.